

On page 76, line 28, please delete "C." and insert in its place --Fig. 48(iii) shows--.

On page 77, line 5, please delete "Figure 50" and insert in its place --Figures 50(i)-(ii)--.

In the Claims

*See amdt B*  
Please cancel claims 1-43.

Please add the following claims.

44. A method of obtaining a specific binding pair member, which method comprises:

expressing in recombinant host cells a library of nucleic acid sequences encoding a genetically diverse population of polypeptides provided by mutating nucleic acid encoding a specific binding pair member which comprises an enzyme or fragment thereof, which enzyme or fragment thereof is able to bind a ligand and is at least 100-200 amino acids, wherein polypeptides encoded within the library are each expressed as a fusion with a coat protein surface component of a filamentous bacteriophage which displays said polypeptides at the surface of bacteriophage particles, there being packaged in each particle a nucleotide sequence encoding a said fusion, whereby the genetic material of each said particle displaying a polypeptide includes a nucleic acid sequence encoding the polypeptide displayed on that particle.

45. A method according to claim 44 wherein said domain or fragment is at least 200 amino acids.

46. A method according to claim 44 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

47. A method according to claim 45 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

48. A method according to claim 44 wherein particles formed by said expression are selected or screened to provide an individual displayed polypeptide specific binding pair member or a mixed population of displayed polypeptide specific binding pair members associated in respective particles with nucleic acid encoding said displayed polypeptide specific binding pair member or members, the specific binding pair member or members thus provided having ability to bind a complementary ligand.

49. A method according to claim 48 wherein the particles are selected by affinity with a complementary ligand.

50. A method according to claim 49 which comprises recovering any particles bound to said complementary ligand by washing with an eluant.

51. A method according to claim 50 wherein the eluant contains a molecule which competes with said particles for binding to said complementary ligand.

52. A method according to claim 49 wherein the particles are applied to said complementary ligand in the presence of a molecule which competes with said particles for binding to said complementary ligand.

53. A method according to claim 48 wherein the particles are selected by enzymatic activity.

54. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48; and

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(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

55. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

56. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49; and

(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

57. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

58. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53; and

(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

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59. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

60. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 48, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

61. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 50 a said derivative specific binding pair member.

62. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 49, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific

binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

63. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 62 a said derivative specific binding pair member.

64. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a selected or screened particle obtained by a method according to claim 53, said nucleic acid encoding a polypeptide specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to a polypeptide specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

65. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 64 a said derivative specific binding pair member.

66. Recombinant host cells harboring a library of nucleic acid sequences comprising sequences encoding a genetically diverse population of polypeptides provided by mutation of a nucleic acid sequence encoding a specific binding pair member which comprises an enzyme or a fragment thereof, which enzyme or fragment thereof is

67. Recombinant host cells according to claim 66 wherein said domain or fragment is at least 200 amino acids.

69. Recombinant host cells according to claim 67 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

71. A particle according to claim 70 wherein said domain or fragment is at least 200 amino acids.

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73. A particle according to claim 71 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

74. A library of filamentous bacteriophage particles including particles according to claim 70 displaying a population of specific binding pair members.

75. A library according to claim 74 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

76. A library of filamentous bacteriophage particles including particles according to claim 71 displaying a population of specific binding pair members.

77. A library according to claim 76 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

78. A method of obtaining a member of a specific binding pair, the method comprising:  
contacting a library of filamentous bacteriophage particles according to claim 74 with a desired ligand, and  
separating particles displaying specific binding pair members which bind to said desired ligand.

79. A method according to claim 78 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

80. A method of obtaining a member of a specific binding pair, the method comprising:

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contacting a library of filamentous bacteriophage particles according to claim 74 with a desired ligand, and  
separating particles displaying specific binding pair members which have a desired enzymatic activity.

81. A method according to claim 80 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

82. A method of obtaining a member of a specific binding pair, the method comprising:

contacting a library of filamentous bacteriophage particles according to claim 76 with a desired ligand, and  
separating particles displaying specific binding pair members which bind to said desired ligand.

83. A method according to claim 82 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

84. A method of obtaining a member of a specific binding pair, the method comprising:

contacting a library of filamentous bacteriophage particles according to claim 76 with a desired ligand, and  
separating particles displaying specific binding pair members which have a desired enzymatic activity.

85. A method according to claim 84 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.



86. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78; and

(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

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87. A method according to claim 86 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

88. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80; and

(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

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89. A method according to claim 88 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

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90. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82; and

(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

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91. A method according to claim 90 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

92. A method of producing a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84; and

(ii) producing by expression from nucleic acid obtained in step (i) the encoded specific binding pair member.

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93. A method according to claim 92 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

94. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

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95. A method according to claim 94 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

96. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

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97. A method according to claim 96 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

98. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

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99. A method according to claim 98 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

100. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a specific binding pair member.

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101. A method according to claim 100 wherein said coat protein surface component is the gene III capsid protein of phage fd or its counterpart in another filamentous phage.

102. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 78, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

103. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 102 a said derivative specific binding pair member.

104. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 80, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

105. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 104 a said derivative specific binding pair member.

106. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 82, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

107. A method of producing a specific binding pair member, the method comprising:

producing by expression from encoding nucleic acid obtained by a method according to claim 106 a said derivative specific binding pair member.

108. A method of producing nucleic acid encoding a specific binding pair member, the method comprising:

(i) obtaining nucleic acid from a separated particle obtained by a method according to claim 84, said nucleic acid encoding a first specific binding pair member or a polypeptide chain component thereof; and

(ii) producing from nucleic acid obtained in step (i) nucleic acid which encodes a derivative specific binding pair member, wherein said derivative specific binding pair member is provided by the addition, deletion, substitution or insertion of one or more amino acids, or by the linkage of another molecule, to said first specific binding pair member or polypeptide chain component thereof encoded by the nucleic acid obtained in step (i).

109. A method of producing a specific binding pair member, the method comprising:

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producing by expression from encoding nucleic acid obtained by  
~~a method according to claim 108 a said derivative specific binding pair member.~~

110. A specific binding pair member obtained by a method according to claim 48.

111. A specific binding pair member obtained by a method according to claim 49.

112. A specific binding pair member obtained by a method according to claim 53.

113. A specific binding pair member obtained by a method according to claim 54.

114. A specific binding pair member obtained by a method according to claim 56.

115. A specific binding pair member obtained by a method according to claim 58.

116. Nucleic acid obtained by a method according to claim 55.

117. Nucleic acid obtained by a method according to claim 57.

118. Nucleic acid obtained by a method according to claim 59.

119. Nucleic acid obtained by a method according to claim 60.

120. Nucleic acid obtained by a method according to claim 62.

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121. Nucleic acid obtained by a method according to claim 64.
122. A specific binding pair member obtained by a method according to claim 61.
123. A specific binding pair member obtained by a method according to claim 63.
124. A specific binding pair member obtained by a method according to claim 65.
125. A specific binding pair member obtained by a method according to claim 78.
126. A specific binding pair member obtained by a method according to claim 80.
127. A specific binding pair member obtained by a method according to claim 82.
128. A specific binding pair member obtained by a method according to claim 84.
129. A specific binding pair member obtained by a method according to claim 86.
130. A specific binding pair member obtained by a method according to claim 88.
131. A specific binding pair member obtained by a method according to claim 90.

132. A specific binding pair member obtained by a method according to

133. Nucleic acid obtained by a method according to claim 94.

134. Nucleic acid obtained by a method according to claim 96.

135. Nucleic acid obtained by a method according to claim 98.

136. Nucleic acid obtained by a method according to claim 100.

137. Nucleic acid obtained by a method according to claim 102.

138. Nucleic acid obtained by a method according to claim 104.

139. Nucleic acid obtained by a method according to claim 106.

140. Nucleic acid obtained by a method according to claim 108.

141. A specific binding pair member obtained by a method according to

142. A specific binding pair member obtained by a method according to

143. A specific binding pair member obtained by a method according to

144. A specific binding pair member obtained by a method according to

In the Drawings

Please substitute the formal drawings submitted herewith for the informal